REMARKS

Claims 8 to 14 are pending in the application; claim 14 has been added with the instant amendment.

Rejection under 35 U.S.C. 102

Claims 8 and 11-13 stand rejected under 35 U.S.C. 102(e) as being anticipated by *Coleman et al. (US 5,665,065)*.

Claim 8 has been amended to define a medicament/dosimeter combination package that comprises a diagnostic indicator system for a patient-specific property that is relevant for the action, side effect, interaction, metabolism, absorption, distribution, metabolism, and elimination of the medicament to be administered to a patient, wherein the patient-specific property is a genetic property that is determined by gene expression testing.

New claim 14 is directed to the gene expression chip.

The concept of gene expression testing is set forth in particular in the specification on page 2, 1st paragraph and 2nd paragraph (at 1.), and in the specific examples 1 to 5 presented in the specification (pages 5 to 7). The gene expression chip is set forth on page 7, line 4.

The system according to the invention is concerned particularly with individual dosing of a medicament, in accordance with the individual genetic properties ("fingerprint") of the patient. In humans, the genetic foundations of many processes occurring within the body, for example, metabolic processes controlled by enzymes, are known. Genes regulate also the activity of cellular enzymes, that inter alia individually determine the metabolic conversion, resorption, and action or side effects of medicaments. In special situations, it can be determined from the "fingerprint" whether taking a certain medicament will even cause a therapeutic effect (responder/non-responder definition). Information obtained in accordance with the present invention by gene expression testing in regard to individual characteristics of cell activity of a patient is employed in order to provide a patient with optimal administration scheme of an appropriate medicament with regard to type, dosage and dosage intervals.

As set forth in the specification (page 2, paragraph beginning at the middle of the page), the invention provides an analytical measuring unit used before taking or dosing a medicament in order to define the genetic type of the patient and to derive therefrom a

conclusion whether the patient is to be treated or not to be treated with a specific medicament or with a specific quantity of a medicament.

As set forth in the preferred embodiments (see examples 1-5 on pages 5 to 7 of the specification), the invention is applied in connection with a responder/non-responder situation where it is determined on the basis of a certain gene expression which therapy concept is to be selected or optimized. This is done e.g. in that in tumor tissue of a female patient the expression of HER2 is measured before beginning a breast cancer therapy with antibodies against HER2. Only when it is determined by gene expression testing that HER2 is over-expressed, the therapy is employed.

As set forth in example 2, an optimization of a desired medication effect is realized while simultaneously side effects are reduced as much as possible. In certain time intervals, a female patient performs an estrogen receptor expression test by means of the indicator system. Based on the measured number of receptors, an individual dosage is calculated. Alternatively, a tumor marker is determined (e.g. M2-PK, CEA, MUCH-1) that indicates the suppression or spreading of metastases of the tumor. In this way, for the temporal course of a long-term treatment the optimal dosage is always made available.

In examples 3 and 4, the invention is explained in connection with lipid lowering substances (statines) and beta-blocker medications (high blood pressure or post-MI).

Example 5 relates to the detection of a genetic predisposition in regard to the enzyme cytochrome P450 that is responsible for the metabolism of antidepressive agents and other drugs. Especially low activity of the enzyme leads to inhibition of the metabolism of the taken antidepressive agents or of other drugs. This can cause dangerously high plasma levels of the drug. On the other hand, a very active metabolism prevents the build-up of an effective blood level and the drug is ineffective. Therefore, with the present invention cytochrome P450 of a patient can be characterized with a gene expression chip directly or indirectly by metabolic conversion of an appropriate substrate. Based on the result, the patient is classified as a slow/fast metabolizer and the dosage of the antidepressive agent is adjusted accordingly.

The gist of the invention is therefore that a sample taken form a patient is measured or tested prior to selecting a therapy or a medication and before determining the dosage of the medication. The gene expression testing provides information in regard to very

specific individual characteristics (i.e., a "fingerprint") of the genetic properties of the patient. The examples presented in the specification refer to gene expression or receptor expression (as a consequence of gene expression).

The fingerprint sets forth personal characteristics of a patient that are genetically defined and not simply reflected by a single blood parameter reading. Instead detection of several genetically imparted parameters is performed on a test chip that is coated with one or several reactive substances and that, after reaction with the applied bodily fluid, provides one or several measurable results. Based on the results, dosage quantities and regimens are proposed or permitted or excluded (see page 3, 3rd paragraph; "gene expression chip" cited on page 7, line 4, of the specification).

The present invention thus concerns diagnostics based of genetic characterization of body fluids or cells collected from the patient prior to starting a medication therapy; monitoring of the effectiveness of the therapy/medication is of course possible also. Testing during the therapy is necessary on special cases where it is known that the gene expression might be affected by the administered drug or the physiological response (receptor up and down regulation).

The invention is thus concerned with the interaction between the medication and the individual to be treated. Based on the patient's gene expression test results that indicate the individual response or constitution of the patient, the dosage is determined or the proper type of medication is selected in a form customized to the patient. As set forth in the specification on page 7, last two paragraphs, patients can be treated individually according to their special needs instead of according to a generalized treatment scheme that is based on statistics and too coarsely incremented. The present invention provides improved efficacy of the medicament because it is adjusted individually. In an ideal situation a significant reduction of side effects can be observed because of the optimization of the dosage as well as of the dosage interval. This improves the chances of curing the patient and also provides improved quality of life for the patient (side effects reduced or eliminated) as well as a reduction of the total costs (no excess quantities of medication are administered) and thus a positive economic effect for the patient and the health-care system. It is also possible to shelter from the beginning so-called non-responders from ineffective treatment that often causes severe side effects.

Coleman et al. teach simply the continuous measuring/monitoring of a blood glucose level by means of a glucose sensor and a device for injecting insulin in accordance with the measured glucose level. This has nothing in common with the claimed combination package with an indicator system based on gene expression testing in order to determine a patient's individual fingerprint for selecting a proper medication and/or dosage before starting a therapy.

Reconsideration and withdrawal of the rejection of claim 8 and its dependent claims are therefore respectfully requested.

Rejection under 35 U.S.C. 103

Claim 9 stands rejected under 35 U.S.C. 103(a) as being unpatentable over *Coleman et al.* and *Gough (US 4,671,288).*

Claim 9 is believed to be allowable as dependent claim of claim 8.

CONCLUSION

In view of the foregoing, it is submitted that this application is now in condition for allowance and such allowance is respectfully solicited.

Should the Examiner have any further objections or suggestions, the undersigned would appreciate a phone call or **e-mail** from the examiner to discuss appropriate amendments to place the application into condition for allowance.

Authorization is herewith given to charge any fees or any shortages in any fees required during prosecution of this application and not paid by other means to Patent and Trademark Office deposit account 50-1199.

Respectfully submitted on November 11, 2008,

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